Remarks

Claims 1-7 are pending in the application. Claims 5-7 have been added. Claims 1, 2, and 3 have been amended. Support for the new claims and claim amendments can be found throughout the application, including the claims as originally filed. Specifically, support for the amendments to claims 1 and 2 can be found on page 23, lines 29-31, and continued onto page 24, lines 1-2 of the specification; page 26, lines 26-31, of the specification; and page 28, lines 7-20, of the specification. Support for new claims 5-7 can be found on page 26, lines 26-31, of the specification and in Examples 3 and 4. Importantly, no new matter has been added to the claims. The amendment to the claims should not be construed to be an acquiescence to any of the rejections. The amendments to the claims are being made solely to put the claims in proper format to expedite the prosecution of the above-identified application. The Applicant reserves the right to further prosecute the same or similar claims in subsequent patent applications claiming the benefit of priority to the instant application. 35 USC § 120.

Response to Rejections under 35 U.S.C. § 102(a)

Claims 1, 3 and 4 stand rejected under 35 U.S.C. § 102(a) based on the Examiner's contention that they are anticipated by Kim et al. (U.S. Patent No. 5,723,147 ("Kim et al. '147")). The Applicants respectfully traverse this rejection.

The Applicants submit that Kim et al. '147 does not anticipate claims 1, 3, and 4 as amended because Kim et al. '147 does not disclose using a polycation as a complexing agent. To anticipate a claim, a single reference must disclose each and every limitation of the claim. *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569 (Fed. Cir. 1984).

Kim et al. '147 discloses a process of preparing a biologically active agent encapsulated within a multivesicular liposome comprising the steps:

a) dissolving in one or more organic solvents a lipid component containing at least one neutral lipid and at least one amphipathic lipid;

b) adding into the lipid component an immiscible first aqueous component containing one or more biologically active substances to be encapsulated;

c) adding a hydrochloride to either or both the first aqueous component and the lipid component, forming a water-in-oil emulsion from the two immiscible components;

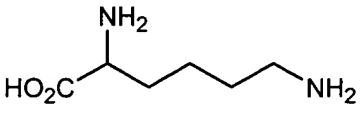
d) dispersing the water-in-oil emulsion with a second aqueous component to form solvent spherules containing in them multiple droplets of the first aqueous component; and

e) removing the organic solvents, such as by evaporation. See col. 1, ll. 37-51.

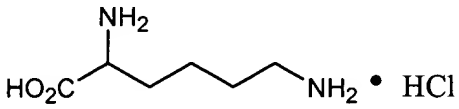
The term hydrochloride is described as being hydrochloric acid or other hydrochlorides such lysine hydrochloride. See col. 3, ll. 51-56.

The Applicants submit that lysine (free base) or lysine hydrochloride, described by the Examiner in the office action as complexing with an active agent, is not a polycation and therefore Kim et al. '147 does not anticipate the claims as amended.

Lysine and lysine hydrochloride are depicted below. Please also see the BASF technology data sheet included with this response for the structure of lysine hydrochloride.



lysine free base

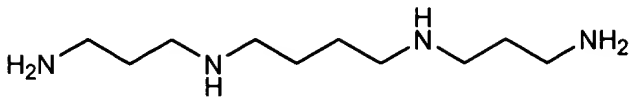


lysine hydrochloride

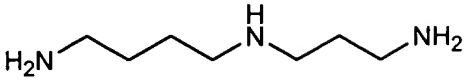
One can see that neither lysine free base nor lysine hydrochloride is a polycation. Lysine free base is not even a cation and lysine hydrochloride is monocationic since there is only one molecule of HCl for every molecule of lysine free base. Even at extremely low pH, lysine · 2HCl would not be polycationic. Polycations are defined in the specification as having three or more ionizable groups. Lysine at most has two potentially ionizable groups that would yield cations.

In contrast, the present claims as amended require that the complexing agent is polycationic such as for example spermine (4 ionizable groups for forming a polycation)

or spermidine (3 ionizable groups for forming a polycation) depicted below.



spermine



spermidine

Because Kim et al. '147 does not disclose polycationic complexing agents, the Applicants submit that Kim et al. '147 does not anticipate the claims as amended.

Accordingly, the Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 102(a).

Response to Rejections under 35 U.S.C. § 102(b)

Claim 1 stands rejected under 35 U.S.C. § 102(b) based on the Examiner's contention that it is anticipated by Kim et al. (Cancer Research, **1993**, *53*, 1596-1598 ("Kim et al. Cancer Paper")). The Applicants respectfully traverse this rejection.

The Applicants submit that, as was the case with Kim et al. '147, Kim et al. Cancer Paper does not anticipate claim 1 because it does not disclose a polycationic complexing agent. To anticipate a claim, a single reference must disclose each and every limitation of the claim. *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569 (Fed. Cir. 1984).

The lysine in Kim et al. Cancer Paper is not a polycation for the same reasons as described above under the Response to Rejections under 35 U.S.C. § 102(a) heading.

Because Kim et al. Cancer Paper does not disclose a polycationic complexing agent, the Applicants submit that it does not anticipate each and every limitation of the claim as amended.

Accordingly, the Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. § 102(b).

Response to Rejections under 35 U.S.C. § 103(a)

Kim et al. (U.S. Patent No. 5,723,147)

Claim 2 stands rejected under 35 U.S.C. § 103(a) based on the Examiner's

contention that it is obvious over Kim et al. (U.S. Patent No. 5,723,147 ("Kim et al. '147")). The applicants respectfully traverse this rejection.

Claim 2 differs from claim 1 in that an emulsion comprising a lipid and a polycationic complexing agent is prepared before adding a bioactive agent, instead of as in claim 1 where an emulsion between a lipid and a bioactive agent is formed before adding a polycationic complexing agent.

However, as discussed above, Kim et al. '147 does not teach a method of preparing a lipid encapsulated bioactive agent comprising a polycationic complexing agent. It would not be obvious from Kim et al. '147 to use a polycationic complexing agent because one of ordinary skill in the art would know from a fair reading of Kim et al. '147, especially where the preferred hydrochloride is HCl, see col. 5, l. 37, that the role of the hydrochloride, even when it is lysine hydrochloride, is to lower the pH. The role is not to condense the bioactive agent as described on page 23, lines 29-31 and continued onto page 24, lines 1-2, of the specification. It would not be obvious to one of ordinary skill in the art to substitute the HCl or lysine hydrochloride of Kim et al. '147 with the polycationic complexing agent of the present claims because there is no motivation in Kim et al. '147 to make such a structurally different substitution.

Because Kim et al. '147 does not teach each and every limitation of claim 2, the Applicants respectfully request the withdrawal of the rejection of claim 2 under 35 U.S.C. § 103(a).

Kim et al. (U.S. Patent No. 5,759,573)

Claims 1-4 stand rejected based on the Examiner's contention that they are obvious under 35 U.S.C. 103(a) over Kim et al. (U.S. Patent No. 5,759,573 ("Kim et al. '573")). The Applicants respectfully traverse this rejection.

The method disclosed by Kim et al. '573 is similar to the method disclosed in Kim et al. Cancer Paper (see Example 1). Importantly, the method disclosed in Kim et al. '573 does not teach using a polycationic complexing agent as required by the amended claims.

Unlike the polycationic complexing agents of the present invention that lead to better packing of the bioactive agent within the liposome, cyclodextrin of Kim et al. '573 acts more like an additional lipid. Cyclodextrin is a cyclic oligomer containing anywhere from 6 to 12 glucose units. The hydrophilic hydroxy groups of the glucose units are directed toward the outside of the molecule leaving a hydrophobic cavity. See col. 4, ll. 48-60. The bioactive agent is associated with the hydrophobic cavity in the same way it is associated with the hydrophobic moiety of a lipid, but it does not form a complex with the cyclodextrin in the same manner as the polycationci complexing agents of the present invention. It also would not have been obvious to one of ordinary skill in the art to substitute the cyclodextran of Kim et al. '573 with the polycationic complexing agents of the present claims because there is no motivation supplied by Kim et al. '573 to make such a structurally different substitution.

Because Kim et al. '573 teaches using cyclodextrin and not a polycationic complexing agent, the Applicants respectfully request the withdrawal of the 35 U.S.C. 103(a) rejection of claims 1-4.

Fees

The Applicants believe they have provided for the required fees in connection with the filing of this paper. Nevertheless, the Director is hereby authorized to charge any additional required fee to our Deposit Account, **06-1448**.

Conclusion

For the foregoing reasons, the Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the pending claims are now in condition for allowance and early notification to this effect is earnestly solicited. If any questions are raised by this Amendment and Response, the Examiner is urged to contact the undersigned at the telephone number listed below.

Respectfully submitted,
Patent Group
Foley Hoag LLP

By: Michael J. DiVerdi

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Agent for Applicants

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Date: 11/30/05

BASF
The Chemical Company

L-Lysine Hydrochloride*
99.5%

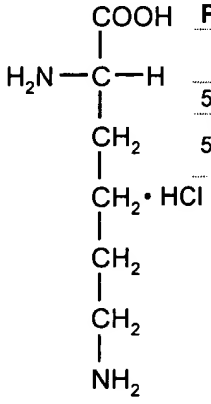
L-Lysine Hydrochloride 99.5% is a white fine powder or granular material, produced by fermentation technology.

Article #	Article Name	Package
56308140	L-Lysine Hydrochloride 99.5%, Fine Powder	25 kg box
56308246	L-Lysine Hydrochloride 99.5%, Granular (U.S. Grade)	25 kg box

The product conforms with the applicable specifications in the current United States Pharmacopoeia (USP) and the Food Chemicals Codex (FCC).

Specifications

Assay... ≥ 99.5% of $C_6H_{14}N_2O_2 \cdot HCl$, dried basis
Loss on drying ..... ≤ 0.4%
Residue on ignition..... ≤ 0.1%
pH (10% aqueous solution) .....5.0 to 6.0
Arsenic .....≤ 1 ppm
Heavy metals as Pb...≤ 10 ppm
Iron .....≤ 30 ppm
Sulfate .....≤ 300 ppm
Chloride content .....19.0% - 19.6%
Organic volatile impurities .....meets the requirements
Specific rotation $[\alpha]_D^{25}$.....+20.4° to +21.4°



Particle Size Specification

		US Sieve#	µm
56308140	min. 95% thru	60	250
56308246	min. 7.5% on	20	850
	max. 40% thru	80	180

Lysine HCl
CAS 657-27-2
$C_6H_{14}N_2O_2 \cdot HCl$
Molecular Weight: 182.6

Characteristics

Stability... When stored in the original unopened container under recommended storage conditions, the shelf life is:
56308140 .....36 months
56308246 .....24 months

Applications...for food and supplement applications.

Storage...store in tightly closed original container in a dry place at temperatures below 25°C.

Packaging...25 kg box.

Country of Origin... South Korea

Note...must handle in accordance with the Material Safety Data Sheet

Bulletin #: HNLYS-10-1204

Human Nutrition
Sales: 800-527-9881
Technical: 800-469-7542
Fax: (973) 245-6843
In Mexico call: 800-723-3000

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